molecular masses of wild-type C_H3 and T366S:L368A:Y407V, T366W and Y407A variants determined by high resolution electrospray mass spectrometry were as expected.

Please replace the paragraph beginning at page 92, line 11 with the following:

Phage were prepared from individual clones following 7 rounds of selection and also from the control vector, pRA1. Briefly, phagemids in XL1-BLUE™ were used to inoculate 25 ml LB broth containing 50 μg/ml carbenicillin and 10 μg/ml tetracycline in the presence of 10^9 pfu/ml M13K07 and incubated overnight at 37 °C. The cells were pelleted by centrifugation (6000 *g*, 10 min, 4°C). Phage were recovered from the supernatant by precipitation with 5 ml 20 % (w/v) PEG, 2.5 M NaCl followed by centrifugation (12000 *g*, 10 min, 4 °C) and then resuspended in 1 ml PBS. 180 μl 0-6 M guanidine hydrochloride in PBS was added to 20 μl phage preparations and incubated for 5.0 min at approximately ~25 °C. Aliquots (20 μl) of each phage sample were then diluted 10-fold with water. The presence of C_H3 heterodimer was assayed by ELISA using 5B6-coated plates and detecting the phage with an anti-M13 polyclonal Ab conjugated to horseradish peroxidase, using o-phenylenediamine as the substrate. The reaction was quenched by the addition of 50 μl 2.5 M H_2SO_4 and the absorbance measured at 492 nm. The absorbance data were plotted against the quanidine hydrochloride concentration during the melt and fitted to a 4 parameter model by a non-linear least squares method using Kaleidagraph™ 3.0.5 (Synergy Software).

Please replace the paragraph beginning at page 94, line 27 with the following:

The phage display selection strategy described herein allows the selection in favor of C_H3 mutants that form stable heterodimers and selection against mutants that form

stable homodimers. The counter selection against homodimers occurs because "free" C_H3 mutants will compete with the flagged C_H3 knob mutant for binding to available C_H3 mutant-gene III fusion protein. The free C_H3 mutants arise as a result of the amber mutation between the natural C_H3 gene and M13 gene III. In an amber suppressor host such as XL-Blue™, both C_H3-gene III fusion protein and corresponding free C_H3 will be secreted.

Please replace the paragraph beginning at page 98, line 7 with the following:

ScFv fragments that bound human leptin receptor (Ob-R) or the extracellular domain of the HER3/c-erbB3 gene product (HER3) were obtained by three rounds of panning using a large human scFv phage library (Vaughan et al. (1996), *supra*). Leptin receptor-IgG and HEr3-IgG (10 μg in 1 ml PBS were used to coat separate Immuno™ tubes (Nunc; Maxisorp™) overnight at 4°C. Panning and phage rescue were then performed as described by Vaughan et al. (1996), *supra*, with the following modifications. A humanized antibody, huMAb4D5-8 (Carter, P. et al. (1992) PNAS USA 89:4285-4289) or humanized anti-IgE (Presta, L. et al. (1993) J. Immunol. 151:2623-2632) at a concentration of 1 mg/ml was included in each panning step to absorb Fc-binding phage. In addition, panning in solution Hawkins, R.E., et al. (1992) J. Mol. Biol. 226:889-896) was also used to identify scFv binding leptin receptor. The leptin receptor was separated from the Fc by site-specific proteolysis of leptin receptor-IgG with the engineered protease, Genenase™ (Carter, P., et al. (1989) Proteins: Structure, Function and Genetics 6:240-248) followed by protein A Sepharose chromatography. The leptin receptor was biotinylated and used at a concentration of 100

nM, 25 nM and 5nM for the first, second, and third rounds of panning, respectively. Phage binding biotinylated antigen were captured using streptavidin-coated paramagnetic beads (Dynabeads™, Dynal, Oslo, Norway).

Please replace the paragraph beginning at page 101, line 20 with the following:

Expression and purification of a bispecific antibody immunoadhesin variants was performed as follows. Human embryonic kidney 293S cells were transfected with three plasmid DNAs, encoding anti-CD3 light chain, anti-CD3 IgG_1 heavy chain or CD4IgG. For each transfection, the ratio of light chain-encoding DNA to heavy chain-encoding DNA was 3:1 so that light-chain would not be limiting for assembly of anti-CD3 IgG. Additionally, because the immunoadhesin is poorly expressed, the ratio of immunoadhesin encoding plasmid was added in excess to heavy chain encoding plasmid. The ratios tested ranged from 3:1:3 through 8:1:3 for immunoadhesin:heavy chain:light chain phagemids. 10 μg total plasmid DNA were then co-transfected into 293S cells by means of calcium phosphate precipitation (Gorman, C., DNA Cloning, Vol II. D. M. Glover, Ed. IRL Press, Oxford, p 143 (1985)), washing cells with PBS prior to transfection. Fc-containing proteins were purified from cell supernatants using immobilized protein A (ProSep A™, BioProcessing Ltd., UK) and buffer-eschanged into PBS. Iodoactemide was added to protein preparations to a final concentration of 50 mM to prevent reshuffling of disulfide bonds.